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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,434	YANG ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *122-157* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *122-157* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/7/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-121 are cancelled.

Claims 122-157 have been added.

2. Claims 122-157 are pending and under consideration to the extent that the antibody is an anti-CD20 antibody or rituximab, i.e., applicants' elected species.

3. This Office Action contains New Grounds of Rejections.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 07 November 2008 have been fully considered by the examiner. A signed and initialed copy of the IDS is included with the instant Office Action.

Objections/Rejections Withdrawn

5. The objection to the specification because the title of the invention is not descriptive is withdrawn in view of the newly submitted title filed 11/7/08.

6. ***All rejections applied to claims 22-81 in the previous Office Action mailed 6/26/08 are withdrawn in view of the cancellation of the claims.***

New Grounds of Rejections

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Newly added claims 122-134, 136-151 and 153-157 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al (U.S. Patent 6,171,586 B1, 6/13/1997, IDS reference 3 filed 12/20/2004) in view of Relton et al (US Patent 6,252,055, 11/12/1998, IDS reference BR filed 5/2/2005).

Lam et al teach the preparation of anti-CD20 antibody compositions, including pharmaceutical compositions comprising an anti-CD20 monoclonal, chimeric or humanized antibody in 5 mM to 30 mM, or 10 mM acetate (e.g., sodium acetate) or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0, which solves the need in the art for a stable aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapeutic use in treating B cell lymphoma patients (see entire document, particularly cols. 2, 5-10, 13-14, 22-2, Example 2 and claims). Lam et al do not specifically teach subjecting the antibody compositions to membrane filtration to produce an antibody composition

having a higher concentration of antibodies than the initial antibody preparation, wherein the concentration of the antibodies is at least 50 mg/ml, or at least 100 mg/ml, or wherein the antibodies of the antibody composition have one or more of the isotypes selected from IgG, IgG_1, IgG_4, IgM, IgA, IgD and IgE. These deficiencies are made up for in the teachings of Relton et al.

Relton et al teach methods for producing concentrated antibody preparations and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, wherein the antibody is a monoclonal, chimeric or humanized antibody and has an isotype selected from IgG_1, IgG_2, IgG_3, IgG_4, IgM, IgA, IgD and IgE and the antibody is specific for a tumor cell marker for human tumor therapy, wherein the method comprises providing an antibody preparation, filtering the antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and leading to the successful concentration of antibody at a concentration of 100 mg/ml or greater, which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody (see entire document, particularly cols. 1-2, 3, lines 18-27, 35-37, col. 5 and claims).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method for producing a concentrated anti-CD20 antibody preparation (e.g., monoclonal, chimeric and humanized anti-CD20 antibodies and having and having an IgG_1, IgG_2, IgG_3, IgG_4, IgM, IgA, IgD or IgE isotype) and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an anti-CD20 antibody preparation comprising anti-CD20 antibodies in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0 and filtering the anti-CD20 antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane

at a reduced circulation rate, thereby reducing sheer stresses and the successful concentration of anti-CD20 antibodies at a concentration of 100 mg/ml or greater for therapeutic benefit in human B cell lymphoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a method for producing a concentrated anti-CD20 antibody preparation (e.g., monoclonal, chimeric and humanized anti-CD20 antibodies and having an IgG_1, IgG_2, IgG_3, IgG_4, IgM, IgA, IgD or IgE isotype) and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an anti-CD20 antibody preparation comprising anti-CD20 antibodies in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0 and filtering the anti-CD20 antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and the successful concentration of anti-CD20 antibodies at a concentration of 100 mg/ml or greater for therapeutic benefit in human B cell lymphoma patients in view of Lam et and Relton et al because Lam et al teach the preparation of anti-CD20 antibody compositions, including pharmaceutical compositions comprising an anti-CD20 monoclonal, chimeric or humanized antibody in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0, which solves the need in the art for a stable aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapeutic use in treating B cell lymphoma patients and Relton et al teach methods for producing concentrated antibody preparations and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an antibody preparation, filtering the antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and leading to the successful concentration of antibody

at a concentration of 100 mg/ml or greater, which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody and wherein the antibody is a monoclonal, chimeric or humanized antibody and has an isotype selected from IgG_1, IgG_2, IgG_3, IgG_4, IgM, IgA, IgD and IgE and the antibody is specific for a tumor cell marker for human tumor therapy. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to concentrate the anti-CD20 monoclonal, chimeric and humanized antibody preparations of Lam et al according to the method of Relton, which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody and also solves the need in the art for a stable aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapy in B cell lymphoma patients. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). See also *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a method for making a concentrated anti-CD20 antibody preparation (e.g., monoclonal, chimeric and humanized anti-CD20 antibodies and having an IgG_1, IgG_2, IgG_3, IgG_4, IgM, IgA, IgD or IgE isotype) and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an anti-CD20 antibody preparation comprising anti-CD20 antibodies in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0 and filtering the anti-CD20 antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and the successful concentration of anti-CD20

antibodies at a concentration of 100 mg/ml or greater for therapeutic benefit in human lymphoma patients in view of Lam et and Relton et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

9. Claims 122, 135, 141 and 152 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al (U.S. Patent 6,171,586 B1, 6/13/1997, IDS reference 3 filed 12/20/2004) in view of Relton et al (US Patent 6,252,055, 11/12/1998, IDS reference BR filed 5/2/2005) and Maloney et al (Blood, 90(6):2188-2195, 1997).

Lam et al have been described supra. Lam et al do not specifically teach subjecting the antibody compositions to membrane filtration to produce an antibody composition having a higher concentration of antibodies than the initial antibody preparation or the chimeric anti-CD20 antibody, rituximab. These deficiencies are made up for in the teachings of Relton et al and Maloney et al.

Relton et al have been described supra.

Maloney et al teach the administration of IDEC-C2B8 chimeric anti-CD20 monoclonal antibody (also known as rituximab) in human non-Hodgkin's lymphoma patients that results in tumor inhibition and according to Maloney et al presents the opportunity to obtain meaningful tumor reductions with minimal toxicity (see entire document, particularly pp. 2188, 2190-2191, 2194 and Fig. 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method for producing a concentrated IDEC-C2B8 chimeric anti-CD20 antibody preparation and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an IDEC-C2B8 chimeric anti-CD20 antibody preparation comprising the IDEC-C2B8 chimeric anti-CD20 antibody in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range

of 4.5 to 6.0, 4.8 to 5.5, or 5.0 and filtering the IDEC-C2B8 chimeric anti-CD20 antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and the successful concentration of the IDEC-C2B8 chimeric anti-CD20 antibody preparation at a concentration of 100 mg/ml or greater for therapeutic benefit in human non-Hodgkin's lymphoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a method for producing a concentrated IDEC-C2B8 chimeric anti-CD20 antibody preparation and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an IDEC-C2B8 chimeric anti-CD20 antibody preparation comprising the IDEC-C2B8 chimeric anti-CD20 antibody in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0 and filtering the IDEC-C2B8 chimeric anti-CD20 antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and the successful concentration of the IDEC-C2B8 chimeric anti-CD20 antibody preparation at a concentration of 100 mg/ml or greater for therapeutic benefit in human non-Hodgkin's lymphoma patients in view of Lam et al and Relton et al and Maloney et al because Lam et al teach the preparation of anti-CD20 antibody compositions, including pharmaceutical compositions comprising a chimeric anti-CD20 antibody in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0, which solves the need in the art for a stable aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapeutic use in treating B cell lymphoma patients and Relton et al teach methods for producing concentrated antibody preparations and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an antibody preparation, filtering the

antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and leading to the successful concentration of antibody at a concentration of 100 mg/ml or greater, which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody and Maloney et al teach that the administration of IDEC-C2B8 chimeric anti-CD20 monoclonal antibody (also known as rituximab) in human non-Hodgkin's lymphoma patients results in tumor inhibition and the IDEC-C2B8 chimeric anti-CD20 monoclonal antibody presents the opportunity to obtain meaningful tumor reductions with minimal toxicity according to Maloney et al. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to produce an anti-CD20 antibody composition comprising the IDEC-C2B8 chimeric anti-CD20 monoclonal antibody of Maloney and concentrate the IDEC-C2B8 chimeric anti-CD20 antibody composition according to the method of Relton, which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody and the IDEC-C2B8 chimeric anti-CD20 monoclonal antibody of Maloney is advantageous in that it reduces tumor burden in non-Hodgkin's lymphoma patients with minimal toxicity. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). See also *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a method for producing a concentrated IDEC-C2B8 chimeric anti-CD20 antibody preparation and pharmaceutical compositions comprising such and a physiologically acceptable carrier or diluent, comprising providing an IDEC-C2B8 chimeric anti-CD20

antibody preparation comprising the IDEC-C2B8 chimeric anti-CD20 antibody in 5 mM to 30 mM, or 10 mM acetate or histidine buffer in the pH range of 4.5 to 6.0, 4.8 to 5.5, or 5.0 and filtering the IDEC-C2B8 chimeric anti-CD20 antibody preparation through a retentate side of a filtering membrane using ultrafiltration to produce a filtrate and recirculating the filtrate back to said retentate side of the filtering membrane at a reduced circulation rate, thereby reducing sheer stresses and the successful concentration of the IDEC-C2B8 chimeric anti-CD20 antibody preparation at a concentration of 100 mg/ml or greater for therapeutic benefit in human non-Hodgkin's lymphoma patients in view of Lam et and Relton et al and Maloney et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Arguments

10. The response filed 11/7/2008 argues (i) one of ordinary skill in the art would not have arrived at Applicants' claimed invention with any sort of predictability and (ii) the superior properties of the claimed invention overcome a *prima facie* case of obviousness, if any.

With respect to (i) applicant states that while Lam et al disclose stable final pharmaceutical compositions comprising 10 mM acetate or histidine, one would not have been motivated from Lam to add a low concentration of acetate or histidine buffer to an initial antibody concentration for the purpose of improving the antibody's properties after membrane filtration. Due to the lack of a filtration step in Lam et al, Applicant states that the ordinary skilled artisan would not have been motivated to further subject Lam's final formulation to a membrane filtration step that removes water and buffer. Applicant also states that like Lam, Relton also fails to recognize the importance of using acetate or histidine to buffer the initial antibody preparation prior to the membrane filtration step and the initial

antibody preparations described in Relton contain citrate buffer as a conventional preparation method. Applicants' arguments have been fully considered but are not found persuasive. "The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985) (The prior art taught combustion fluid analyzers which used labyrinth heaters to maintain the samples at a uniform temperature. Although appellant showed an unexpectedly shorter response time was obtained when a labyrinth heater was employed, the Board held this advantage would flow naturally from following the suggestion of the prior art.). In the instant case, the teachings of Lam et al indicate that 5 mM to 30 mM, or 10 mM acetate or histidine buffer provide a stable aqueous pharmaceutical formulation of anti-CD20 antibodies, which solves the need in the art for a stable aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapeutic use in treating B cell lymphoma patients and Relton et al teach methods for producing concentrated antibody preparations which reduce sheer stresses, leading to the successful concentration of antibody at a concentration of 100 mg/ml or greater, and which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to concentrate the anti-CD20 monoclonal, chimeric and humanized antibody preparations of Lam et al according to the method of Relton, which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody and also solves the need in the art for a stable concentrated aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapy in B cell lymphoma patients. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been

produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). The fact that applicant has recognized that the use of 2 mM to about 48 mM acetate or histidine buffer improves stability and viscosity of concentrated antibodies after membrane filtration, however, this advantage would flow naturally from following the suggestion of the prior art as discussed supra. Additionally, Applicant is reminded that obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). Applicant has failed to overcome the *prima facie* case of obviousness.

Applicants' arguments regarding the citrate buffer of Relton et al make little sense, since Lam et al already teach that acetate or histidine buffer provide a stable aqueous pharmaceutical formulation of anti-CD20 antibodies and applicant has not provided a logical rationale or sound scientific reasoning why one of ordinary skill in the art would remove the acetate or histidine buffer from the stable aqueous pharmaceutical formulation of anti-CD20 antibodies of Lam et al and introduce citrate buffer prior to filtration. As noted by Applicant, Lam et al teach that acetate or histidine buffer provide a stable aqueous pharmaceutical formulation of anti-CD20 antibodies.

With respect to (ii) Applicants' arguments and evidence showing that the acetate or histidine buffer decreases turbidity and viscosity of the concentrated antibody, relative to the citrate buffer have been fully considered but are not found persuasive. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979) (Claims were directed to grooved carbon disc brakes wherein the grooves were provided to vent steam or vapor during a braking action. A prior art reference taught noncarbon disc brakes which were grooved for the purpose of cooling the faces of the braking members and eliminating dust. The court held the prior art references when combined would

overcome the problems of dust and overheating solved by the prior art and would inherently overcome the steam or vapor cause of the problem relied upon for patentability by applicants. Granting a patent on the discovery of an unknown but inherent function (here venting steam or vapor) "would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art." 596 F.2d at 1022, 201 USPQ at 661.); *In re Baxter Travenol Labs.*, 952 F.2d 388, 21 USPQ2d 1281 (Fed. Cir. 1991) (Appellant argued that the presence of DEHP as the plasticizer in a blood collection bag unexpectedly suppressed hemolysis and therefore rebutted any *prima facie* showing of obviousness, however the closest prior art utilizing a DEHP plasticized blood collection bag inherently achieved same result, although this fact was unknown in the prior art.). As discussed supra, Lam et al already teach stable aqueous pharmaceutical formulations of anti-CD20 antibodies in 5 mM to 30 mM, or 10 mM acetate or histidine buffer, which solves the need in the art for a stable aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapeutic use in treating B cell lymphoma patients and Relton et al teach methods for producing concentrated antibody preparations which reduce sheer stresses, leading to the successful concentration of antibody at a concentration of 100 mg/ml or greater, and which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to concentrate the anti-CD20 monoclonal, chimeric and humanized antibody preparations of Lam et al according to the filtration method of Relton, which overcomes the art recognized problems of low recovery rates and precipitate formation when concentrating antibody and also solves the need in the art for a concentrated stable aqueous pharmaceutical formulation comprising an anti-CD20 antibody suitable for therapy in B cell lymphoma patients, and hence, the combined prior art would inherently overcome the turbidity and viscosity problem relied upon for patentability by applicant.

Accordingly the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejections are maintained.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643